

ABSTRACT

[0118] The methods and apparatus disclosed herein concern nucleic acid sequencing by enhanced Raman spectroscopy. In certain embodiments of the invention, nucleotides are covalently attached to Raman labels before incorporation into a nucleic acid. In other embodiments, unlabeled nucleic acids are used. Exonuclease treatment of the nucleic acid results in the release of labeled or unlabeled nucleotides that are detected by Raman spectroscopy. In alternative embodiments of the invention, nucleotides released from a nucleic acid by exonuclease treatment are covalently cross-linked to nanoparticles and detected by surface enhanced Raman spectroscopy (SERS), surface enhanced resonance Raman spectroscopy (SERRS) and/or coherent anti-Stokes Raman spectroscopy (CARS). Other embodiments of the invention concern apparatus for nucleic acid sequencing.